



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 03-APR-2001

SUBJECT: PP# 6E06167. Diflubenzuron (Dimilin™ 2L, EPA Reg #400-461) in/on Pears. **Evaluation of Residue Data and Analytical Methods.** MRID#s 451196-01 and -02. Chemical 108201. Barcode D272978. Case 293100. Submission S590172.

FROM: George F. Kramer, Ph.D., Chemist *George F. Kramer*
Registration Action Branch 1 (RAB 1)
Health Effects Division (HED) (7509C)

THRU: G. Jeffrey Herndon, Branch Senior Scientist *G. Jeffrey Herndon*
RAB1/HED (7509C)

TO: Shaja Brothers/Robert Forrest, PM Team 5
Registration Division (RD) (7505C)

Interregional Research Project No. 4 (IR-4) requests the establishment of the following permanent tolerances for the insect growth regulator diflubenzuron (DFB), expressed as the combined residues of DFB [N-[[[4-chlorophenyl]amino]carbonyl]-2,6-difluorobenzamide] and its metabolites convertible to 4-chloroaniline (PCA):

Pears 0.5 ppm

A temporary tolerance is established for residues of DFB and its metabolites convertible to PCA in rice grain at 0.01 ppm [40 CFR 180.377(a)(2)]. Permanent tolerances are established for residues of the insecticide DFB in or on the following raw agricultural commodities (RACs): cottonseed at 0.2 ppm; grapefruit at 0.5 ppm; mushrooms at 0.2 ppm; orange at 0.5 ppm; soybean at 0.05 ppm; tangerine at 0.5 ppm; walnuts at 0.1 ppm; fat, mby, and meat of cattle, goats, hogs, horses, sheep at 0.05 ppm; milk at 0.05 ppm; poultry fat, mby, meat at 0.05 ppm; and eggs at 0.05 ppm [40 CFR

180.377(a)(1)]. There are also regional tolerances established in or on pasture grass at 1 ppm and range grass at 3 ppm [180.377(c)].

Executive Summary of Chemistry Deficiencies

- Revise Section B to prohibit the use of oil in the late-season treatments.
- A successful Petition Method Validation (PMV) of analytical enforcement methods for crops.

CONCLUSIONS

OPPTS GLN 860.1200: Proposed Uses

1. The petitioner has adequately described the rates and timings of the proposed use.

OPPTS GLN 860.1300: Nature of the Residue - Plants

2a. The qualitative nature of the residue in plants is adequately understood based on data from citrus, mushroom, rice and soybean metabolism studies.

2b. The HED Metabolism Assessment Review Committee (MARC) has concluded (Memo, Kramer & Reddy, in preparation; D272976) that the residues of concern are DFB and its metabolites PCA and 4-chlorophenylurea (CPU).

OPPTS GLN 860.1300: Nature of the Residue - Livestock

3. As there are no livestock feed items currently associated with pears, issues pertaining to the nature of the residue in livestock are not germane to this petition.

OPPTS GLN 860.1340: Residue Analytical Methods

4. Adequate methods are available for the analysis of DFB in pears. Three enforcement methods for DFB are published in PAM, Vol. II as Methods I, II, and III. Method II is a GC/ECD method that can separately determine residues of DFB, CPU, and PCA in eggs, milk, and livestock tissues. All three methods have undergone successful PMVs and are acceptable for enforcement purposes. Individual analyte methods for have been submitted for CPU and PCA. The methods and Independent Laboratory Validations (ILVs) have been sent to the Analytical Chemistry Laboratory (ACL) for a PMV (Memo, J. Rowell 12/15/98; D251484). HED will withhold

a final conclusion on the adequacy of these methods as analytical enforcement methods pending receipt of the PMV reports. However, these methods are based on Method II. HED thus has no objections to a conditional registration while the PMV of the methods for PCA and CPU in rice commodities is performed.

OPPTS GLN 860.1360: Multiresidue Method

5. The FDA PESTDATA database dated 1/94 (PAM Vol. I, Appendix II) contains no information on DFB recovery using Multiresidue Methods PAM, Vol. I Sections 302, 303, and 304. However, the registrant has submitted Multiresidue testing data that the Agency has forwarded to the FDA (Memo, L. Edwards 9/17/93; D194722). Also, the results of Multiresidue Method testing of PCA and CPU have been submitted and forwarded to FDA (Memo, J. Rowell 12/15/98; D254273). Neither PCA nor CPU were adequately recovered.

OPPTS GLN 860.1380: Storage Stability Data

6a. The RAC samples from the field residue studies were stored for a maximum of 9 months prior to analysis for DFB, for a maximum of 10 months prior to analysis for CPU and for a maximum of 7 months prior to analysis for PCA. The storage intervals for DFB in the storage stability study are significantly shorter than those of the field residue samples. However, residues of DFB have been shown to be stable in a variety of RACs for up to 12 months of storage (DFB Reregistration Eligibility Decision RED, 3/16/95). The requirements for DFB storage stability data on pears is thus satisfied.

6b. PCA and CPU are unstable, degrading significantly after 1 and 3 months, respectively. Therefore, for magnitude of residue samples with storage periods greater than 1 month for PCA and 3 months for CPU, correction factors could be used in order to determine the residue levels that were present at the time of sample collection. However, in the case of the pear trials submitted with this petition, residues of DFB were 1-4 orders of magnitude greater than that of PCA and CPU. Correction of the PCA and CPU residues for degradation during storage would thus not have a significant effect on the results of the pear magnitude of the residue study.

OPPTS GLN 860.1500: Crop Field Trials

7. HED notes that the maximum observed residue, 1.58 ppm, exceeds the proposed tolerance of 0.5 ppm. However, oil was mistakenly added to the finished spray for the late-season treatments in this trial, thus invalidating the results. The number and geographic distribution of the acceptable pear trials are sufficient. The petitioner has provided data from a total of 8 field residue trials conducted in Regions 1 (1 trial), 10 (3 trials), 11 (3 trials) and

12 (1 trial). These results support the proposed tolerance of 0.5 ppm, provided the label is amended to prohibit the use of oil in the late-season treatments. **A revised Section B is required.**

OPPTS GLN: 860.1520: Processed Food/Feed

8. As there are no processed commodities associated with pears, processing studies not are required to support the subject petition.

OPPTS GLN 860.1480: Meat, Milk, Poultry, Eggs

9. As there are no livestock feed items currently associated with pears, issues pertaining to the magnitude of the residue in livestock are not germane to this petition.

OPPTS GLN 860.1850 and 860.1900: Confined/Field Accumulation in Rotational Crops

10. As pears are a perennial crop, confined and field rotational crop studies are not required to support the subject petition.

Other Considerations

11. The Codex Alimentarius has established a maximum residue limit (MRL), expressed in terms of diflubenzuron *per se*, of 1 ppm on pear. Therefore, as the U.S. residue definition includes CPU and PCA, compatibility is not possible with the proposed tolerance. A copy of the IRLS (International Residue Limit Status) sheet is attached to this memorandum.

RECOMMENDATIONS

Provided Section B is revised as specified in Conclusion 7, HED concludes there are no residue chemistry data requirements that would preclude the establishment of the proposed permanent tolerances for residues of DFB in/on pears. Registration of Dimilin[™] should be made conditional upon successful Agency validation of analytical enforcement methods for PCA and CPU in crops as specified in Conclusion 4. A human-health risk assessment will be prepared as a separate document.

Note to RD: The tolerance should be expressed as "the combined residues of diflubenzuron [N-[[[4-chlorophenyl]amino]carbonyl]-2,6-difluorobenzamide] and its metabolites 4-chloroaniline and 4-chlorophenylurea" in/on "pear" at "0.50 ppm."

DETAILED CONSIDERATIONS

OPPTS GLN 860.1200: Proposed Uses

The petitioner provided specimen labels for a 2 lb./gal flowable concentrate (FlC) formulation (Product name = DIMILIN[™] 2 L Insect Growth Regulator; EPA Reg. No. 400-461) and a 25% wettable powder (WP) formulation (Product name = DIMILIN[™] 25W Insect Growth Regulator; EPA Reg. No. 400-465) proposed for use on pears. Dimilin may be applied at a use rate of 0.125-0.75 lbs. ai/A using a minimum spray volume of 80 gal/A. Up to 4 applications are allowed per season with a seasonal maximum use rate of 1.0 lb. ai/A. The minimum pre-harvest interval (PHI) is 14 days. Surfactants or oil (0.25-1%) may be added to the finished spray. The petitioner has adequately described the rates and timings of the proposed use.

OPPTS GLN 860.1300: Nature of the Residue - Plants

The qualitative nature of the residue in plants is adequately understood based on data from citrus, mushroom, rice and soybean metabolism studies.

In the mushroom metabolism study, compost was spawned with mushroom culture and then was treated with DFB at 1x (4/22/87, CBTS #2085). Residues of DFB, CPU, difluorobenzoic acid (DFBA), and 4-chloroaniline (p-chloroaniline, PCA) were detected at levels up to 0.18, 0.60, 4.0, and 0.02 ppm respectively. The tolerance for DFB in/on mushrooms is 0.2 ppm. If DFB were present in/on mushrooms at the tolerance level, combined residues of CPU and PCA could be present at 0.69 ppm.

The vast majority of the residue in citrus fruit is composed of unchanged parent compound, and no detectable levels (<1 ppb) of PCA, CPU, or DFBA were present (Memo S. Knizner, 3/16/95).

In the soybean metabolism study, >90% of the TRR in soybean leaves was unchanged parent (ppm levels not provided). DFBA, CPU, and PCA were not detected, but the limit of detection (LOD) for these compounds was not provided. In soybean hulls, 81.4% to 97.9% of the TRR (6.57 -17.5 ppm) was identified as unchanged parent. Again, DFBA, CPU, and PCA were not detected. The LOD for these compounds was 0.3 ppm. Residues in soybean seeds were too low to allow for metabolite characterization (<0.1 to 0.038 ppm) (Memo S. Knizner, 3/16/95).

The major component of the TRR in rice straw was the parent DFB (42% of the TRR, 3.77 ppm) (Memo G. Kramer, 6/23/98; D240107). CPU, as the free metabolite, comprised 28.6% of the TRR, its

conjugated form in soluble form accounted for 2.5%, and CPU bound to insolubles accounted for ~10%. In rice grain, DFB accounted for 0.3% of the TRR (0.002 ppm). The major metabolite in grain was CPU present in its free form (~20% of the TRR, 0.132 ppm). DFB in rice is metabolized via cleavage of the urea linkage to CPU, and DFBA (2,6-difluorobenzoic acid); only very small concentrations of PCA are formed. The metabolism of DFB in rice grain is similar to that in cotton and citrus, and the radioactive components are also similar to those found in soil.

The HED MARC has concluded (Memo, Kramer & Reddy, in preparation; D272976) that the residues of concern are DFB and metabolites PCA and CPU.

OPPTS GLN 860.1300: Nature of the Residue - Livestock

As there are no livestock feed items currently associated with pears, issues pertaining to the nature of the residue in livestock are not germane to this petition.

OPPTS GLN 860.1340: Residue Analytical Method - Plant Commodities

Adequate methods are available for the analysis of DFB in pears. Three enforcement methods for DFB are published in PAM, Vol. II as Methods I, II, and III. Method II is a GC/ECD method that can separately determine residues of DFB, CPU, and PCA in eggs, milk, and livestock tissues. All three methods have undergone successful PMVs and are acceptable for enforcement purposes. Individual analyte methods for have been submitted for CPU (LOQ of 0.001 ppm) and PCA (LOQ of 0.005 ppm). A detailed description of these procedures has been provided previously (Memo G. Kramer, 6/23/98; D240107). The methods and ILVs have been sent to the ACL for PMV (Memo, J. Rowell 12/15/98; D251484). HED will withhold a final conclusion on the adequacy of these methods as analytical enforcement methods pending receipt of the PMV reports. However, these methods are based on Method II. HED thus has no objections to a conditional registration while the PMV of the methods for PCA and CPU in rice commodities is performed.

OPPTS GLN 860.1340: Residue Analytical Methods - Livestock Commodities

As there are no livestock feed items currently associated with pears, issues pertaining to residue analytical methods in livestock are not germane to this petition.

OPPTS GLN 860.1360: Multiresidue Method

The FDA PESTDATA database dated 1/94 (PAM Vol. I, Appendix II) contains no information on DFB recovery using Multiresidue Methods PAM, Vol. I Sections 302, 303, and 304. However, the registrant has submitted Multiresidue testing data that the Agency has forwarded to the FDA (Memo, L. Edwards 9/17/93; D194722). Also, the results of Multiresidue Method testing of PCA and CPU have been submitted and forwarded to FDA (Memo, J. Rowell 12/15/98; D254273). Neither PCA nor CPU were adequately recovered.

OPPTS GLN 860.1380: Storage Stability Data

Storage stability data were submitted with the field residue data (MRID# 451196-02). Samples of pears were spiked with DFB (0.05 ppm), CPU (0.10 ppm) or PCA (0.10 ppm) and analyzed with the methods described above after 1-12 months of storage (Table 1).

Table 1: Summary of Storage Stability for Control Pear Samples Spiked with DFB, PCA or CPU.

Compound	Residue Level (ppm)	Storage Period (Months)	Average Fresh Fortification Recovery (%)	Average Apparent Recovery in Stored Sample (%)	Average Corrected Recovery in Stored Sample (%)
DFB	0.05	0	75.7	NA	NA
	0.05	1	75.2	74.0	98.4
	0.05	2.5	69.6	72.5	104.1
CPU	0.1	0	103.4	NA	NA
	0.1	1	88.0	85.5	97.1
	0.1	3	95.6	96.1	100.5
	0.1	6	99.4	31.6	31.8
PCA	0.1	0	96	NA	NA
	0.1	1	85	40	47
	0.1	3	111	23	20
	0.1	6	114	24	21
	0.1	12	100	14	14

HED's Conclusion: The RAC samples from the field residue studies were stored for a maximum of 9 months prior to analysis for DFB,

for a maximum of 10 months prior to analysis for CPU and for a maximum of 7 months prior to analysis for PCA. The storage intervals for DFB in the storage stability study are significantly shorter than those of the field residue samples. However, residues of DFB have been shown to be stable in a variety of RACs for up to 12 months of storage (DFB RED, 3/16/95). The requirements for DFB storage stability data on pears is thus satisfied.

PCA and CPU are unstable, degrading significantly after 1 and 3 months, respectively. Therefore, for magnitude of residue samples with storage periods greater than 1 month for PCA and 3 months for CPU, correction factors could be used in order to determine the residue levels that were present at the time of sample collection. However, in the case of the pear trials submitted with this petition, residues of DFB were 1-4 orders of magnitude greater than that of PCA and CPU. Correction of the PCA and CPU residues for degradation during storage would thus not have a significant effect on the results of the pear magnitude of the residue study.

OPPTS GLN 860.1500: Crop Field Trials

Submitted with this petition:

Diﬂubenzuron: Magnitude of the Residue on Pear. MRID# 451196-01.

A total of 7 field residue trials were conducted in 1997 in 4 different states plus Canada. These trials were located in Regions 1 (1 trial), 10 (2 trials), 11 (2 trials) and 12 (1 trial). At each site, two treated plots were established. In treatment 1, pears were harvested at normal maturity following a single application of DFB (Dimilin 25W) at the bud stage of ~0.75 lb ai/A (0.75X the maximum proposed application rate) and a PHI of 112-184 days. In treatment 2, pears were harvested at normal maturity following 4 applications of DFB (Dimilin 25W), each of ~0.25 lb ai/A (1X the maximum proposed application rate), at PHIs of 77, 56, 35 and 14 days. The spray volume was 100-268 gal/A. Dormant oil was added to the finished spray for treatment 1. Oil was not added to the finished spray for treatment 2, except for the Canadian trial where oil was mistakenly used. Two replicate samples were harvested from each treated plot. Total storage time from harvest to analysis was 208-274 days (DFB analysis), 159-286 days (CPU analysis) and 138-203 days (PCA analysis). Samples were analyzed for residues of DFB and its metabolites CPU and PCA using GC/ECD or GC/MSD as described above. The methods were validated over a range of 0.005-1.2 ppm. The average recoveries were 75-103 ± 6-16%. Residues of DFB, CPU and PCA were each <LOQ in/on all pear samples from treatment 1 (LOQs for DFB, CPU and PCA are 0.05 ppm, 0.001 ppm and 0.005 ppm, respectively). Maximum residues of DFB, CPU and PCA

were 1.57 ppm, 0.025 ppm and <0.005 ppm, respectively in/on pear samples from treatment 2 (Table 2).

Submitted with this petition:

Diﬂubenzuron: Magnitude of the Residue on Pear. MRID# 451196-02.

A total of 2 field residue trials were conducted in 1996 in 2 different states. These trials were located in Regions 10 (1 trial) and 11 (1 trial). At each site, two treated plots were established. In treatment 1, pears were harvested at normal maturity following 2 applications of DFB (Dimilin 25W) of ~0.25 lb ai/A (1st) and ~0.25 lb ai/A (2nd) (1X the maximum proposed application rate), at PHIs of 84 and 63 days. In treatment 2, pears were harvested at normal maturity following 4 applications of DFB (Dimilin 25W), each of ~0.25 lb ai/A (1X the maximum proposed application rate), at PHIs of 84, 63, 35 and 14 days. The spray volume was 50 gal/A. Three replicate samples were harvested from each treated plot. Total storage time from harvest to analysis was 68-75 days (DFB analysis), 175-178 days (CPU analysis) and 292-298 days (PCA analysis). Samples were analyzed for residues of DFB and its metabolites CPU and PCA using GC/ECD or GC/MSD as described above. The methods were validated over a range of 0.001-2.0 ppm. The average recoveries were 76-91 ± 7-10%. Residues of CPU and PCA were each ≤LOQ in/on all pear samples from treatment 1 (LOQs for DFB, CPU and PCA are 0.05 ppm, 0.001 ppm and 0.005 ppm, respectively), residues of DFB, 0.060-0.118 ppm. Maximum residues of DFB, CPU and PCA were 0.318 ppm, 0.005 ppm and <0.005 ppm, respectively in/on pear samples from treatment 2 (Table 2).

Table 2. Residues of DFB and its metabolites CPU and PCA in/on pears harvested 14 days following the last of 4 application of the 25% WP ~0.25 lb ai/A (1X maximum rate).

Trial Site	EPA Region	Spray Volume (gal/A)	Residues (ppm)			Total
			DFB	CPU	PCA	
MRID# 451196-01						
Parlier, CA	10	231-246	0.170, 0.102	0.004, 0.004	<0.005, <0.005	<0.179, <0.111
Parlier, CA	10	231-246	0.138, 0.175	<0.001, 0.002	<0.005, <0.005	<0.144, <0.016
Wenatchee, WA	11	161-247	0.182, 0.199	0.004, 0.003	<0.005, <0.005	<0.191, <0.207
Wenatchee, WA	11	165-247	0.267, 0.317	0.005, 0.008	<0.005, <0.005	<0.277, <0.330
Alton, NY	1	100	0.234, 0.224	0.016, 0.025	<0.005, <0.005	<0.255, <0.254
Vineland, ON	-	100	1.572, 1.544	<0.001, <0.001	<0.005, <0.005	<1.578*, <1.560*
Hood R., OR	12	174-215	0.351, 0.321	0.006, 0.004	<0.005, <0.005	<0.361, <0.330
MRID# 451196-02						
Upper Lake, CA	10	50	0.180, 0.211, 0.318	0.001, 0.001, 0.002	<0.005, <0.005, <0.005	<0.186, <0.217, <0.325
Zillah, WA	11	50	0.252, 0.237, 0.097	0.002, 0.005, 0.004	<0.005, <0.005, <0.005	<0.259 <0.247, <0.106

* Oil was mistakenly added to the finished spray for the late-season treatments in this trial, thus invalidating the results.

Conclusions: HED notes that the maximum observed residue, 1.58 ppm, exceeds the proposed tolerance of 0.5 ppm. However, oil was mistakenly added to the finished spray for the late-season treatments in this trial, thus invalidating the results. The number and geographic distribution of the acceptable pear trials are sufficient. The petitioner has provided data from a total of 8 field residue trials conducted Regions 1 (1 trial), 10 (3 trials), 11 (3 trials) and 12 (1 trial). These results support the proposed tolerance of 0.5 ppm, provided the label is amended to prohibit the use of oil in the late-season treatments. **A revised Section B is required.**

OPPTS GLN 860.1520: Processed Food/Feed

As there are no processed commodities associated with pears, processing studies not are required to support the subject petition.

OPPTS GLN 860.1480: Meat, Milk, Poultry, Eggs

As there are no livestock feed items currently associated with pears, issues pertaining to the magnitude of the residue in livestock are not germane to this petition.

OPPTS GLN 860.1850: Confined Accumulation in Rotational Crops

As pears are a perennial crop, confined and field rotational crop studies are not required to support the subject petition.

Other Considerations

The Codex Alimentarius has established a MRL, expressed in terms of diflubenzuron *per se*, of 1 ppm on pear. Therefore, as the U.S. residue definition includes CPU and PCA, compatibility is not possible with the proposed tolerance. A copy of the IRLS sheet is attached to this memorandum.

Attachment 1- IRLS Sheet

cc: Kramer
RDI: G. Herndon(4/3/01), RAB1 Chemists (4/3/01)
G.F. Kramer:806T:CM#2:(703)305-5079:7509C:RAB1

INTERNATIONAL RESIDUE LIMIT STATUS			
Chemical Name: N-[[[4-chlorophenyl]amino]carbonyl]-2,6-difluorobenzamide	Common Name: Diflubenzuron	<input checked="" type="checkbox"/> Proposed tolerance <input type="checkbox"/> Reevaluated tolerance <input type="checkbox"/> Other	Date: 3/23/01
Codex Status (Maximum Residue Limits)		U. S. Tolerances	
<input type="checkbox"/> No Codex proposal step 6 or above <input type="checkbox"/> No Codex proposal step 6 or above for the crops requested		Petition Number: 6E06167 DP Barcode: D271495 Other Identifier:	
Residue definition: diflubenzuron		Reviewer/Branch: G.F. Kramer	
		Residue definition: parent and its metabolites convertible to 4-chloroaniline	
Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
pear	1.	Pears	0.5
Limits for Canada		Limits for Mexico	
<input type="checkbox"/> No Limits <input type="checkbox"/> No Limits for the crops requested		<input type="checkbox"/> No Limits <input type="checkbox"/> No Limits for the crops requested	
Residue definition:		Residue definition:	
Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)
Notes/Special Instructions:.			
S. Funk, 03/26/01. Info on Canada and Mexico not available at this time.			

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Rev. 1998



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Chemical:	Diﬂubenzuron
PC Code:	108201
HED File Code	11000 Chemistry Reviews
Memo Date:	04/03/2001
File ID:	DPD272978
Accession Number:	412-02-0010

HED Records Reference Center
01/04/2002

